# Urticaria

**Def:** Transient skin or mucosal swelling due to leakage of plasma. Superficial swelling (wheel)/ deep (angioedema).

**Aetiopathogenesis:**

1)Idiopathic .  2) Mast cell dependent.

3) Mast cell independent urticarial.

## *Mast cell dependent*

**Activation of mast cell** → **By** →
- Immunologic: union of 2 IgE by allergen or autoantibody
- Non immunologic (mast cell releasing agent e.g: substance p, c5a , drugs(codine, morphine, aspirine, cipro,rifampicine).

↓

**Mast cell degranulation and release of mediators**

↓

**Effect of mediators** →
- histamine : itching, flare, erythema,wheals.
- Tryptase,chymase: help in pathogenesis ofurticaria
- PGs+ leukotries:inflammation
- Cytokines: amplify,prolong the wheel

## *Mast cell independent urticarial:*

Direct stimulation of mast cell by:

- Drugs:peneciline, aspirin, NSAIDS.

-food:strawberry, milk, fish.

-infection:tonsillitis, UTI, sinusitis.
-diseases: LE, cancer,thyrotoxicosis.
-physical: heat, cold, pressure.

## Types of urticaria:

1- Ordinary (spontaneous) urticaria(acute-chronic)

2- physicalurticaria(inducible).

3-urticarialvasculitis.

4- contact urticaria.

5- Angioedema without wheels.

6- Distinctive urticarial syndrome:
Papular urticaria+ **Murkle well's syndrome**[urticaria,amylodosis,deafness] + familial mediterrnean fever + **Schnitzler's syndrome** (urticarial vasculitis+ monochlonalgammopathy + fever, bonache + lymphadenopathy)].

## (1)Ordinary urticaria



wheels any where - Last for few – fade within 24hr with normal skin – lesions are very itchy, rubbing than scratching – may associate with erythroderma.

Causes of ordinary urticaria:

Acute<6 weeks: • **Idiopathic** • **URTI** • **Drugs during 1st 36 hrs** •**Food .**

Chronic>6 weeks: •**idiopathic** •**autoimmune** • **pseudo allergic dt ↓ PGE2.** •**Infection.**

Association of chronic urticaria:

- autoimmune→thyroditis, LE, vitiligo.
- infection→ H. pylori.
- Malignancy

**Histopathology:**perivascular lymphocytic inflammatory infilterate – dermal edema

***By EM***: dermal mast cells with signs of degranulation.

## (2)Physical urticaria

Types:

***(!) physical urticaria due to chemical stimuli:***

**a- dermographism=skin writing:** trauma→release Ag→ interact with IgE→degranulation of mast cell→ release of mediators.

Exaggerated physiological response of the skin by stroking by sharp objects→ triple response:- red line: due to dilated capillaries.

- Spreading flare: after 30 sec dt arteriolar dilatation.
- Wheel: dt edema dt ↑capillary permeability.

**Types: i-**immediate (simple,symptomatic). ii- Delayed.





**b- delayed pressure urticaria:**

Sustained skin pressure→ itchy wheel last for 6-48 hrs.

**c-vibratory angioedema[ inherited- acquired]** dt vibratory stimuli.

***(!!) urticaria due to temperature changes:***

**a- heat urticaria:** itchy wheelin response to heat above 34c eg:hot water or warm sunlight.

**b-cold contact urticaria:-**

♦ primary→associated with systemic symptoms (headache, syncope,abd.pain).

♦secondary→ due to serum abnormalities eg: cryoglobulinemia,
cryofibrinogenemia.
Associated with raynoud's or purpura.
Underlying causes→HBV-HCV,infectious mononucleosis.

♦Reflex cold urticaria

♦Familial cold urticaria

***(!!!) urticaria due to sweating or stress:***

**a-cholinergic urticaria:** small micropapular wheel associated with sweating wheather induced by heat or emotion, gustatory stimuli→taste.

- It's due to release of acetyl choline at the sympathetic nerve endings→release of histamine from mast cell.

R/ antihistamine + anticholinergic drugs.

**b- adrenergic urticaria:**small itchy macules or papules within minutes of emotional upset or coffee. Due to release of noradrenaline( histamine, serotonine, dopamine are normal).

**c- exercise induced urticaria:**exercise induced anaphylaxis.

***(!!!!) solar urticaria:***

Wheels develop on exposure to sun light or artificial radiation, it develop within minutes and fade within 1hour

**D.D:**polymorphic light eruption (develop with several hours and fade in longer time).

***(!!!!!) Aquagenicurticaria:***

Urticaria due to contact with water due to reaction to a water soluble Ag in horny layer→diffuse into dermis→histamin release from mast cell.

## (3) Contact urticaria syndrome:

Wheals appears when a substance applied to contact skin it may be:

| Non immunological | immunological |
|---|---|
| - No prior sensitization | - IgE sensitization is required |
| - Due to ↑PGD2 rather than histamine release cause can be blocked by NSAIDs | - dt direct release of most cell mediators. – less common than non imm. |
| Causes: cosmotics, food, occupational exposure to ammonium per sulfate in hairdressers. | - type I HS reaction<br>- causes: latex gloves, food, Milk, nuts, fish. |

**→ Black henna tattoos reaction:**

- **Henna** contains PPD(paraphenylenediamine) and kerosine or petrol is added to ↑uptake of color.
- The reaction appears 7-14 days after exposure for 1st time and only 48 hrs. for 2nd time.
- Lesion: erythema, eczematous, lichenoid, urticarial, pustular or even blistering reactions.



# Treatment of urticaria:

i. **Non drug therapy:-** Re assurance

- Cooling lotion eg: calamine
- avoidaggrevating factors( drugs as NSAIDS, ACE inhibitors , ↓stress, over eating, alcohol.
- Diet: 1- exclusion diet→ food coloring.

2- low pseudo- allergen diet→innn responsive idiopathic.

ii. **Drug therapy:**

1st line : H1 antihistamine if no response combine H1+H2

2nd line: oral steroid( prednisolone) 0.5- 1 mg/kg/day in acute and emergency.

-anabolic steroids →stanozolol in refractory urticaria

-mast cell stabilizers: β -agonist terbutalin, Nifidibine( ca channel antagonist)+ H1 antagonist.

- Narrow band phototherapy.

3rd line:- immunotherapy for sever or non responsding urticaria

- plasmapheresis.
- Cyclosporine 2.5-3.5 mg/kg/day – 3 months.
- Omalizumab (anti IgE antibody).
- Others (methotrexate, mycophenolatemofetil).
-

iii. **Emergency treatment:**

For anaphylaxis or angioedema→respiratory distress.

**Epineprine:** I.M or SC. Rapidaly acting by vasoconstriction, mast cell stabilizer by β-adeno receptor stimulation.

# Angioedema

Subcutaneous variant of urticaria leading to edema of eye lid, lips, genitalia.





**Clinical types:**

1- **Idiopathic**: angioneuroticangio edema.

2- **Drug induced**: ACE inhibitors start after 3 weeks of R/ or any time, may cause laryngeal involvement.

It's mechanism: accumulation of bradykinin through inhibition of kininase II.

3- **Idiopathic angioedema é eosinophilia.**

4- **Hereditary angioedema** : A. Dominant.

- Trigger factors: trauma, infection, stress.
- Associated with: deficiency of natural C1 estrase inhibitor that lead to→ activation of C1 →activation of C4,C2→↑ vaso permeability.
- 2 types
  - Type I → ↓C1 estrase inhibitor level; ↓ C1 inhibitor function.
  - Type II → normal C1inhibitor level; ↓ C1 inhibitor function.

5- **Acquired angioedema:**

Associated with mono clonal gammopathy.

↓ C1 inhibitor level, ↓C1 inhibitor function, ↓C19 level.

Types :- Aquired type I: Immune complex mediated C1, C1 inhibitor consumption

Acquired type II: Anti C1 inhibitor antibodies.

**Treatment of angioedema( Hereditary):**

i. Anabolic steroid: danazol 200-600 mg/day or Stanazolol 1-5 mg/ day.
ii. Epsilon amino caproic acid 12-18 g/ day.
iii. Purified preparation of the inhibitor : the treatment of choice in sever attack.
iv. Replacement therapy: fresh frozen plasma.
v. Icatibantand ecallantide →selective kallikrein inhibitor.

→Bradykinin B2receptor antagonist.

# Eczema

**Endogenous**

- Atopic dermatitis
- Seborric dermatitis
- Hand eczema
- Eczymatous drug eruption
- Eye lid eczema
- Discoid eczema.
- Asteatolic eczema.
- Pitryasisalba.
- Venous eczema.

**Exogenous**

- contact eczema
- photo allergic eczyma
- eczematous poly morphic lighteruption.
- infective eczema.
- post-traumatic eczema
- dermatophytide.

**c/p:** poly morphism : 1ry lesion : papule, macule, vesicle.

2ry lesion: oozing, fissure, crusting.

Not sharply demarcated- itching is common.

**Histopathology:**

| **Acute** | **Subacute** | **Chronic** |
|---|---|---|
| • Spongiosis<br>• Inter, intra cellular edema<br>• Mononuclear cellular<br>• Infilterate in upper<br>• Dermis extend to epidermis(exocytosis) | • Spongiosis<br>• intra cellular edema<br>• acanthosis<br>• parakeratosis<br>• crusting<br>• inflammatory infiltrate | •Marked spongiosis<br>•elongation of rete riges<br>•hyper kertosis parakertosis<br>•inflammatory infiltrate.<br>•fibrosis |

# Seborrheic dermatitis

Chronic inflammatory diseases characterized by red sharply marginated lesions covered with greasy scales mainly in scalp, eye brow, nasolabial fold, ears, axilla (seborrheic sites).

Mainly in males- common in adults.

**Causes:**

(1) malassezia yeast: due to

a- Immunogenic reaction : high antibody for malassezia+ altered cell – mediated immunity.

b- Non immunogenic (irritant): malassezia toxic metabolites lipase, ROS.

(2) surface lipids is the factor not the amount: pt with SD have ↑TG + ↑cholesterol ↓squalene + ↓ FFA.

(3)Emotional stress and endocrinal abnormalities.

**Clinical features:**





**(1)** **Pityasis capitis:** the mildest and commonest.

a- Pityriasis sicca (dandruff) perifollicular redness and scaling which may extend to eye and frontal hair line “corona seborriheica”,Or post auricular. The main complain is itchy scalp.

b- Pityriasis oleosa: oily type.

**(2)** **Diffuse erythema and greasy scales in seborrheic sites.**

**(3)** **Sebo psoriasis:** features of both Ps.,SD.

**(4)** **Generalized SD:** can progress to erythroderma.

- Associations of SD: HIV + parkinsonism, DM, Epilepsy.
- Resistant SD is a sign of:→ HIV
  →Mood disorders.
  → Parkinsonism.
  So the most important IX for resistant cases is HIV investigation:
  1- CD4 lymphocyte count → Reduced
  2- ELISA → for detection of HIV antibodies
  3- PCR → for detection of HIV RNA.

**SD of infancy:** 1 week after birth.





**C/p:** - cradle cap.

- Body lesions: flexural diaper, trunk areas.
- leiner's disease:→non familial( erythroderma desquamatium) generalized self limited SD.

  →Familial: fatal (generalized SD + diarrhea + recurrent infection + ↓weight till death.

  Because of C5 dysfunction and Humoral Immunity dysfunction.

| Psoriasis | Seborrheic dermatitis |
|---|---|
| **St. corn.:**para keratosis + munro micro abscess. | Para keratosis + few pyknotic neutrophils similar to munromicroabscess |
| **Granular layer:**absent or reduced. | Normal granular cell layer |
| **St. spong:** regular acanthosis , elongated rete ridges+ lower clubbing + supra papillary thining + edema of dermal papillae. Exocytosis of lymphocyte, neutrophilis in epidermis. | Irregular acanthosis. Spongiosis (the big diff.) |
| **Dermis:** perivascular infiltrate. | Superficial perivascular infilterate. Perifollicular lymphocytic infiterate. |

## ***Treatment***

**Adult**

-Avoid alcohol based preparation

-oral erythromycin or Flumox for 2ry bacterial infection.

-scalp: frequent shampoo using That contain: tar (poly tar)
Zinc pyrithione(Ultrex)
Salicylic acid in presistant cases

-Glabrous skin:- topical CST or antibact. combination.
-calcineurin inhibitors.
-UVB
- short course of systemic antifungal.

-Generalized SD: - prednisolone 30 mg/day.
-Isotretinon.

**child**

- avoid irritation
- avoid strong keratolytics
- emollients.
- ketoconazol 2%shampo
- short term low potent CST topically for inflammation.

## Dyshidrosis (pompholyx):

- Acute vesico-bullous eruption (sago-like) affect palm and sole. Very sever itching.
- May be due to active fungus infection=Trichophytid.
- Hyper hidrosis may aggrevatepompholyx.

Some pt treated with Botox →improve pomphlyx.

R/ topical + systemic CST

Calcium inhibitors – Bath PUVA.

## Pityriasis alba:

Chronic eczema of unkown origin. Common in children, affect face- start as reddish, irregular ill definedpatch,with fine scales.

R/ topical CST- topical Tacrolimus- pimecrolimus.

# Hand eczema

**Aetiology**

- Infection : tinea(koh) staph(gram stain)
- Endogenous : immunologic(atopic dermatitis)
  idiopathic discoid eczema(pompholyx)
- Exogenous: Irritant contact: chemical (soap)
  Physical(trauma- friction- cold)
  drugs -infection
  - contact allergy (rubber).

**Morphological types:**

- Patchyvesiculo-squamous eczema.
- discoid eczema
- Wear and tear (house wifes and cleaners).
- Ring eczema
- hyper keratotic palmar eczema.
- Recurrent focal palmar peeling( desquamation without itching or vesicle).
- Finger tip eczema: dry skin, cracked, painful fissure.



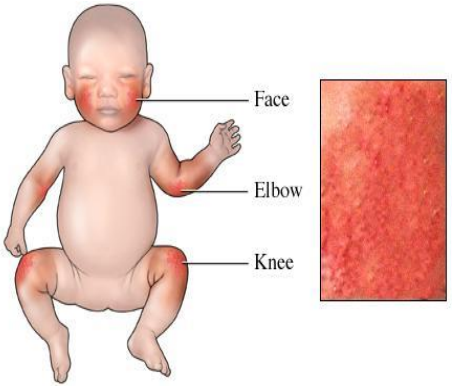


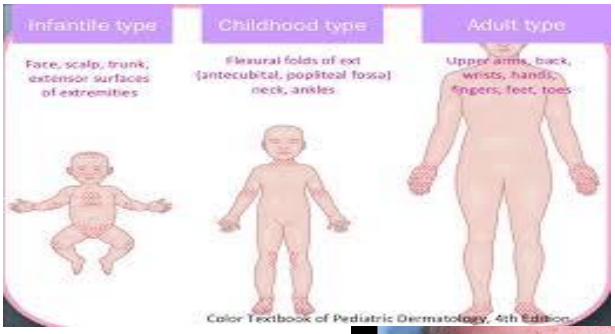
# Atopic dermatitis

Eczematous eruption that is pruritic,recurrent,in flexural areas and Symmetric distribution, common in children and associated with family history of atopy ( asthma- eczema- hay fever).

Early onset→ 1st 2 years - late onset → after puberty

Senile onset →after 60 years.










**C/P:** itching is the cardinal symptom.

* Infantile (2m-2years) cheeks- forehead.
  edematous, erythematous patches covered with vesicles→ exudate→ crust formation.
* Child (2years- 12 years)flexural surface (limb- neck)
  Itchy papules + lichenoid plaques.
* Adult (atopic- neurodermatitis) the same of childhood.

## Regional variants of AD:



- Cheilitis sicca: dryness + fissuring of vermillion lips + fissuring of angular chelitis. The patient trys to moist lips by licking → more irritation of skin around mouth so called lip licker eczema.
- Ear eczema - eye eczema - head and neck
- plantardermatosis -hand eczema. - nipple.

## Ocular manifestation of AD:

(1) Eye lid→swelling, erythema, scalling, ectropion,lichenification, thickening, blepharitis, bacterial,viral colonization, madrosis (lash loss), trichinosis (lash mis direction).

(2) Ocular findinds → conjunctival

Erythema + swelling- symblepharon

Limbal papillae – keratoconus- ant., post.Supcapsular cataract – corneal erosion, ulcer , neovascularization, scarring.

## Aetiopathogenesis of AD:

1- Genetic 2- environmental 3- immunological

4- Epidermal barrier dysfunction.

**(1)Genetic :**+ ve family history(more with disease mother)

Monozygotic twins 77% > dizygotic twins 15%.

2 types of genes: a- epidermal protiens encoding gene(skin only) ex: fillaggrin, SPINK5 →↓ epidermal barrier.

b-protien with immunological function encoding gene.

**(2)Environmental factors**: pollution, infection and others.

-pollution →ulter skin barrier → make it more liable to infection.

-staph.aurus colonization due to : 1- ↓epidermal barrier.

2- ↓level of antimicrobial peptides

3-↑bact. Adherence to skin.

-other triggering factors (allergen →house dust,mites, pollens)
(sweating- harsh soap- cigarette- stress- food(egg, milk, fish))

**(3)Immune response:**

innate immunity:↓ antimicrobial peptide production in skin.

Acquired immunity (acute(TH2 cytoykines), chronic(TH1 cytokines)).

**(4)Epidermal barrier dysfunction:**

Dry scaly skin in lesional, non lesional areas + inflammation of skin due to enviromentalirritant due to:

a- ↓↓fillaggren protein which is responsible for keratin filament aggregation.

b- Disturbed maturation of lamellar bodies.

c- Change in balance bet. Proteolytic enzymes and their anti proteases → ↑ protease activity → barrier dysfunction.

***Diagnosis of atopic dermatitis:*** *3 major + 3 minor*

| **Major criteria** | **Minor criteria** |
|---|---|
| 1- pruritis<br>2-Typical morphology + distribution:<br>a- Flexural lichenification in child, adult.<br>b- Facial, extensors in infancy.<br>3-Personal or family history: AD, Asthma, Allergic rhinitis<br>4-Chronic or chronically relapsing dermatitis | •Xerosis • pityriasisalba<br>• Cheillitis • scaly scalp<br>•nipple eczyma<br>• periauricular eczema<br>•↑IgE •dermographism<br>•Itching when sweating<br>•tendency of cut.Infection. |

**Treatment of atopic dermatitis:**

1- General measures: -explaine the disease
   - Avoid (cats,dogs)(penicilline,aspirin)(stress,soap)
   - Water loose cotton clothes,avoid wool.

2- Topical therapy: - Emollients.
   - Topical steroids
   - Immuno modulators (tacrolimus-pinecrolimus)in moderate or sever or resistant cases dt(more effective + ↓atopy)
   - Coal tar 1-10 % in lichenfication lesions.
   - Anti septic or antibiotic cream for bct. Infection.
   - Cream form for sub acute or acute and oint. Form for chronic cases.

3- Systemic therapy:

- Anti histamine(sedating to break Itch – scratch cycle)
- Treatment of 2ry infection:
  Bact.→antibiotic systemic+ topical
  fungal→ dermatophyte syst.+ topical antifungal
  viral →eczema herpeticum→Acyclovir.
- Systemic corticosteroids (prednisone).
- Sever resistant forms:
  Methotrexate 7.5 – 25 mg/week.
  Azathioprine 2 – 3.5 mg/kg/week.
  Mycophenolatemofetil 2g/daily.
  Narrow band UVB (311 nm).
  PUVA.

# Contact dermatitis

| | Irritant contact dermatitis | Allergic contact dermatitis |
|---|---|---|
| **Incidence:** | 80% | 20% |
| **Causes** | Irritants→chemicals,<br>Acids, alkalies, oil, soap,<br>Detergent. | allergens→Nicle, gold, rubber,<br>topical(Neomycine,bacitran). |
| **Pathogenesis** | Irritants cause dermatitis by direct toxic effect<br>on skin cells leading to their<br>damage.<br>-no immunological memory/<br>No perior sensitizer<br>-it occur to every bodyif the<br>amount and duration are enough.<br>-Irritant cause damage to<br>keratinocytes→release of cytokines(PG2, TNFα, IL1,6,8)→<br>Inflammation cascade.<br>-inflammation occurs at the site<br>Of exposure only. | Delayed type IV HS reaction:<br>1- Antigen processing& presentation<br>most environmental allergen of the low molecular weight(hapten)<br>-hapten can penetrate intact skin→they must combined with larger molecule to be allergen.<br>-they bind to HLA-DR molecule on the surface of APCs (Langerhans).<br>-APCs process the antigen, migrate to regional LNs to meet T-cells.<br>2-Sensitization: In LN,CD4 Tcellrecognize , processes Ag in association é MHCH while CD8 Tcell recognize Ag é MHCD, this<br>Lead to generation of memory cells.<br>3-2ry exposure: 2ry exposure to the same Ag even low amount<br>→inflammatory reaction occurs quickly 24-48hs<br>Inflammation occur at the site of exposure and away from it. |

**Skin lesion for both ICD, ACD:**

Pruritic: acute →clear fluid in bulla or vesicle on red erythematous skin.
Sub acute →less edema + papules.
Chronic →minimal edema + scaling + fissuring+ lichen ficasia

**R/ the same of AD.**

# Erythroderma

The presence of erythema and scaling involve more than 90% of the skin surface

## causes

**adult**

- Psoriasis (erythrodermic type)
- Eczema (erythrodermic(CD,SD,AD))
- Drug reaction(penicillin, barbiturates, Arsenic)
- Idiopathic erythroderma 1-SSSS+ early (chronic-relapsing-severpruritis-PRP Dermatopathic lymphadenopathy esp. in elderly.
- Sézary syndrome, lymphoma.
- Bullous diseases: PNP "para neoplastic", p. foliaceous,BP
- Norwegian scabies.
- LP. – PRP
- Paraneoplastic erythroderma.

**children**

- Icthyosis
- dermatitis(AD,SD)
- psoriasis.
- S.E of infection:
- congental S
- erythrodermic Candidiasis

## Clinical features.

**(1) Cutaneous manifestations:**

→it may be 1ry (erythema with scaling) or 2ry (generalization of local skin disease e.g:psoriasis, AD

→scale: exfoliate 2-6 days in acute phase (large, crusted)
Chronic(small, drier).

***Signs and symptoms***:-pruritus 90% -lichenification1/3 of pt

- Dys pigmentation (hyper >hypo)
- PPK
- Nail changes: shinning, brittleness,dullness, discoloration, paronychia, total shedding.
- Diffuse non- scaring alopecia.

- Eye: bilat. Ectropion+ purelent conjunctivitis.
- Bacterial colonization

**(2)Systemic manifestation:**

a- Generalized lymphadenopathy b-hepatosplenomegaly

c-anaemia(iron def.). d- taclycardia→HF.

e-fluid electrolyte imbalance f-hypo albuminemia

g-thermo regulatory disturbance(hyper>hypothermia)

h-highcrdiac output heart failure, due to ↑BF through skin or ↑ fluid loss.

Complication:systemic manifestation +bacterial colonization

## Diagnosis

(1) initial site involvement.

(2) Clinical findings (3) histopathology

(4)associated systemic manifestation.

(5) history.

## Treatment of erythroderma

(1) Hospitalization

(2) Correct fluid, electrolyte imbalance.

(3) Nutritional support.

(4) Regulate (control) thermia.

(5) R/ of bact. Infection.

(6) Sedating antihistaminics.

(7) Topical R/ :- wet dressing , emollients.

- mild CST oint.

-high potency CST in lichenoid lesions.

(8) R/ of idiopathic erythroderma:

- oral steroid prednisolone(1-2 mg/kg/day)

Maintainance 0.5 mg/kg/day.

Caution during tapering to avoid rebound.

-topical CST + emollients

- oralantihistaminics

(9) Refractory cases:

Cyclosporine 5mg/kg/day then (3-1 mg/kg/day).

# *Prurigo nodularis*

Chronic intensely pruritic nodular disease.

**Aetiology** : un known but:- 80% of pt have atopy.

- 20% of pt follow insect bite.
- Emotional stress may ↑the case.

**C/P: age:** any age but common in elderly.

Site: common in arms, legs, shoulders.bilateral symmetrical.

Size : from small papules to globular nodules, with raised warty surface and a ring of hyperpigmentation around nodules.

- The skin shows slight xeroderma.
- There is crisis of itching and formation of new nodules from time to time .

– pruritus is present.




**D.D:**

(1) Hyper trophic LP.

(2) Pemphigoidnodularis

(3) prurigo of systemic disease.

**Histopathology:**

* **epidermis**: marked hyper keratosis - acanthosis

- Down ward projection of epidermis→pseudo-epitheliomatoushyperplasia.

* **Dermis** : dense infl.infilterate - neural, vascular hyperplasia

- ↑mast cells, merkel cell, ↑eosinophils, neuropeptid – substance P.

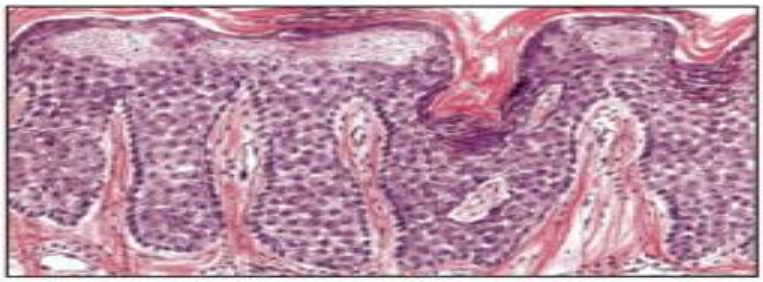


Fig. 2. Histopathology of nodular prurigo in aquarelle. There is hyperkeratosis, parakeratosis, a very marked acanthosis and an epidermal necrosis due to picking. (Courtesy of Dr A. Bjornberg and Dr E. Tegner.)

**Treatment:**

(1) general measures to prevent itching (cut nail)(gloves in sleep).

(2)Topicl capsaicin cream(↓stores of neuro peptides).

(3) Emollients (4) menthol (5) topical anaesthetic

(6) Calcipotriol is more effective than topical CST

(7) Intra lesional CST (kenacort).

(8) Systemic antihistaminic (sedating)

(9) Doxepin (tricyclic antidepressant- anxiolytic- antihistaminic- anti cholinergic).

(10) Gabapentin – cyclosporine- Azathioprine.

(11) Others(PUVA – cryo).

| | **Acute generalized pustular psoriasis (AGPP)** | **Acute generalized exantematous pustules(AGEP)** |
|---|---|---|
| **Cause** | - Pregnancy<br>- rapid trapping of systemic CST or decrease dose<br>-infection<br>-topical Irritant -intensive topical CST. | Most commonly reaction to drug commonly antibiotic eg: Amoxicillin – Ampicillin. |

| | | |
|---|---|---|
| **Clinically:** | -Prodromal symptoms(burning pain).<br>-Fever, malaise.<br>-Pre-exciting psoriasis lesion become fiery red.<br>-Sheet of erythema with tiny pustules that may become confluent (lack of pus).<br>- Mainly in flexures.<br>- Pustule resolve with scaling<br>-Nail →thick,onycholysis by subungual lack of pus. | - Pustulosis develop within 24h of administration of the drug.<br>- Rapid dissemination.<br>- Fever.<br>- Start on face then in flexures |
| **H/P** | **as psoriasis:**<br>-large accumulation of neutrophils : in st.corneum (munro microabscess) Or in st.spinosum(pustules of kogoj)<br>-lymphocytic infilterate with neutrophils. | -Subcorneal or intra-epidermal pustules.<br>- Papillary dermal edema and Lymphohistocytic infilterate é eosinophils.<br>- Vasculitis or single cell keratinocyte necrosis may be present |
| **Prognosis:** | Fatal without effective treatment | Self limited disease. |

# *Fixed drug eruption*

It means that the eruption is recurrent on the same site or sites each time the drug adminesterd.

**Clinically:** the eruption is sharply marginated rounded or oval erythematous patch which become dusky violaceous in colour, some times bullae develop→rupture →erosions. On healing it leaves slate blue pigmentation.

**Site:** penis – lips – dorsa of hand.

Many lesion→generalized FDE ……D.D (E.M & SJS).





**Clinical variants:**

a- Non pigmenting: large diameter> 10 cm. common with pseudo ephiderene It occurs in girdle region.

b- Linear FDE: rare.

**Common drugs causing FDE:**

- Sulphonamide 75% - NSAIDS - tetracyclines

**H/P:** As EM.

(1) Hydropic degeneration of basal cells→pigmentary incontinence.

(2) Bullae may be seen (detachment of dermis,epidermis)

(3) Scattered dyskeratotic keratinocytes, with eosinophilic cytoplasm + pyknoticn+uclei (civatte bodies).

**Histogenesis:**

causes of pigmentery incontinence:

Migration of lymphocytes into epidermis→damage of keratinocytes and become dyskeratotic→ phagosized by macrophagesexcept their melanosomes, cause it is not digested. Then macrophage return to dermis with the phagosizeddyskeratotic cell + melanosomes.

**Treatment of FDE:**

(1) Stop the drug.

(2) ↑ excretion of the drug.

(3) Anti histamine.

(4) Systemic CST in sever cases.

# *Erythema multiform*

Acute self limited mucocutaneous syndrome, recurrence feature.

**Age** : any age - male> female.

**Causes**:un known but:

- **Infection**: HSV 90% - HBV – TB – Leprosy.
- **Drugs**: sulphonamides + orl contraceptive pills.
- **Auto-immune, vascular disease**: DM +LE + poly arteritis nodosa.
- **Malignancy**: cancer, leukemia.
- **Pregnancy, progesterone dermatitis.** - **X ray therapy .**
- **Sarcoidosis.** - **Idiopathic.**

**Pathogenesis:** is unkown but may be due to immunological mechanism.

IF studies show: IgM,C3 in superficial dermal vessels in new lesions (1st 24 hrs)

Auto antibodies against Desmoplakin.

↑ incidence with HLA- AW33, HLA-DQW3.

**EM. Minor:** Typical lesion + rarely atypical+ rare M.M affection.

Bilateral, symmetricl, acute (7-10 days)

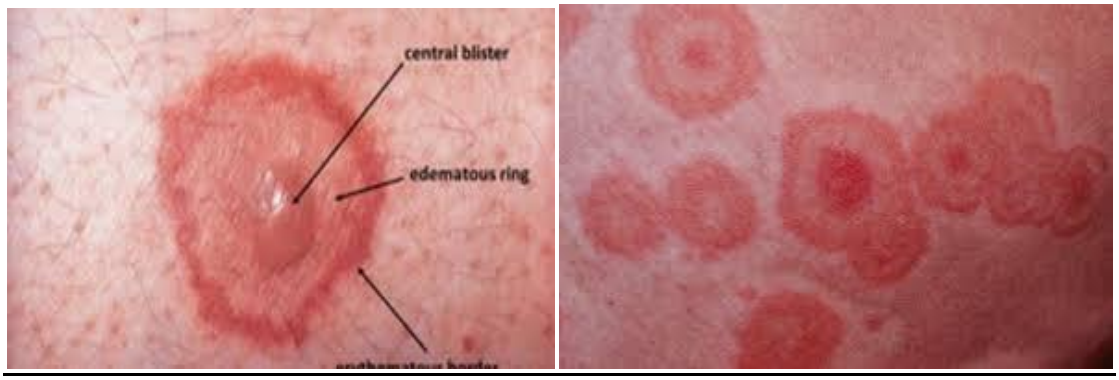
Target lesion: typical 3 zones.(papule)

1st central zone: dusky red or crusted (bull's – eye)

2nd zone: pale. 3rd zone: rim of erythema.

Atypical lesion: 2 zones papule poorly defined border.

Or flat macule 2 zones + poorly defined border.




**EM Major:** typical + atypical +bullous + sever MM affection it's a sever form.

**C/P:** fever, malaise, arthralgia, generalized bullous formation, maculopapular lesions which are confluent + sever affection of oral mucosa in the form of extensive bulla→ rupture→ erosions.

Other organs affected: eye:catarrhal, purulent conjunctivitis

Genital, renal, lung affection.

5 – 15 % of un treated cases →death.

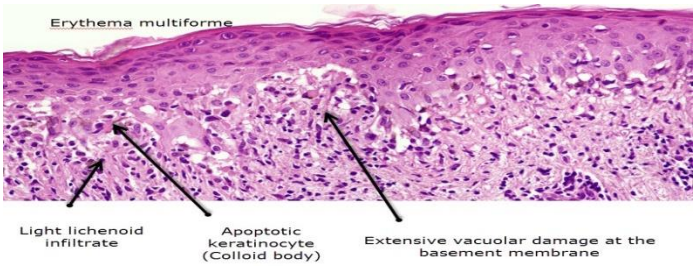
**Histopathology:**

**(1) Epidermis**

- Focal eosinophilic necrosis of keratinocytes - spongiosis
- Vascular degeneration of basal cells lead to bullae formation (sub epidermal) é the basement membrane in floor of bullae.

**(2) Dermis**

Perivascular MN infiltrate + edema of upper dermis + extra vasation of RBCs.




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**Diagnosis:** - skin + m m affection

- Acute + self limited.
- Typical, fixed skin lesions > 7 days
- Target lesion

**D.D** 1- Urticaria : central skin is normal

Transient not fixed-lasts less than 1 day

2- Bullous pemphigoid

**Treatment of EM:**

- R/ of HSV if associated (acyclovir, valacyclovir 0.5- 1gm/day, Famcyclovir 250 1*2).
- R/ of acute eruption:

  2ry infection→ Antibiotic

  Major cases→ Systemic steroids (prednisolone)

# *Steven Johnson syndrome (SJS)/ Toxic epidermal Necrolysis*

They are rare, acute, life threating mucocutaneous disease that's usually drug releated.

**Causes**: (1) drugs 80% :sulphonamide-NSAIDS-Allopurinol-Ampicillin.

(2)Infection: HSV

(3) Neoplasm : Hodgkin's, leukemia

(4) Idiopathic (5) SLE.

**Predisposing factors:**

slow acetylator genotypes.

Immune compromised pt(HIV)- radiotherapy, anticonvulsants, genetic susceptibility.

**Pathogenesis:**

Exposure to a certain types of drugs to predisposing patients lead to immunological reaction to the drug or its metabolites leading to activation of some cell types and cytokines. e.g: Fasl molecule and granulysin from cytotoxic T-cell and NK cells leading to keratinocyte Apoptosis + epidermal necrosis + detachments.

**Clinical features:**

onset: several hours- days start by fever, malaise, skin tenderness, arthralgia then→ erythema which is morbilliform or diffuse + +veNikolsky's sign then→ flaccid bullae → detachment of large areas of necrotic epidermis leaving large, raw painful areas.

SJS < 10% SJS/TEN 10-30% TEN>30%

- Mucous membrane is involved –ocular conjunctivitis in 85% of pt.
- Complete heling without scaring over 2 weeks.
- It occurs by re-epitelializationfrom proliferation and migration of keratinocytes from (reservoir sites)such as healthy epidermis + hair follicles.
- Scarring occurs with 2ry bacterial infection(eye- nail- mm)

**Complication:**

(1) Systemic: acute tubulr necrosis, GN, Bronchopneumonia, GIT bleeding

(2) Imperfect healing:

- eye→conjunctivalsynechiae, entropion, ingrowth of eye lash.
- skin→scarring, depigmentation.
- M.m→persistant erosion, phimosis, vaginal synechaie
- Nail dystrophy – diffuse hair loss.

(3) Mortality rate (25-70%) cause of death is :

- Infection(staph aureus, p. aeruginosa)
- Fluid loss, Electrolyte imbalance.
- Respiratory distress. – multiple organ failure.

**Histopathology:** as EM with:

- Extensive eosinophilic necrosis of epidermis + the cleave above BM.
- Dermis: very little inflammation.

**D.D:** SSSS

**Treatment:**

**Supportive R/:**

Hydration + nutrition + thermoregulation bed

Avoid 2ry infection.

**Specific R/:**

- Cyclosporine 3-4 mg/kg/day.
- Plasmapheresis.
- N – acetyl cysteine.
- IvIg contain antibodies against Fas that able to block binding of Fasl to Fas.
- Systemic CST is remain the mainstay of therapy.